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Secondary hyperparathyroidism causing increased jaw bone density and mandibular pain: a case report

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We present the case of a 32-year-old male patient complaining of recurrent mandibular pain for 3.5 years. Panoramic radiography indicated increased cortical density of the mandibular lower border. Scintigraphy and single-photon emission computed tomography revealed metabolic hyperactivity in that region without pathologic lymph nodes. A bone biopsy specimen of the mandibular lower border did not have inflammation or cytologic atypia. Endocrinologic investigation confirmed secondary hyperparathyroidism as a result of hypovitaminosis D. Several weeks after starting therapy with oral vitamin D supplements, the symptoms completely disappeared. Increased cortical density is a rare manifestation of secondary hyperparathyroidism, which normally causes the lamina dura to vanish and produces a ground-glass appearance as a result of blurring of the trabecular bone pattern. Because focal hyperostosis can have multiple benign or malignant causes, radiologic examination of the jaw bones is indispensable for evaluating orofacial pain. Increased cortical density may be caused by metabolic diseases, requiring further investigations, including biopsy and blood analysis. (Oral Surg Oral Med Oral Pathol Oral Radiol 2017;■■:■■–■■)

Orofacial pain is a common complaint in the dental and maxillofacial field. It can have a variety of causes, including infection, benign and malignant neoplasia, and metabolic diseases. Although orofacial pain mostly is due to a local process, one should always rule out a systemic cause. This is especially true when no evident local lesion can be found.

One such systemic cause may be endocrinologic in origin—that is, hyperparathyroidism. The parathyroid hormone (PTH) regulates serum calcium concentration and bone metabolism. PTH level increases when the serum calcium concentration is low, such as when calcium intake is lacking or when very low vitamin D levels inhibit sufficient enteral calcium uptake, and in the case of chronic kidney disease.[1,2]

In general, PTH attempts to elevate serum calcium levels by stimulating renal calcium reuptake, enteral calcium uptake, and bony calcium release. The effects of PTH can vary according to the age of the patient, the serum PTH concentration pattern, and the skeletal site. Persistently elevated PTH levels generally have catabolic effects, whereas intermittent increases may be anabolic.[1]

The bony alterations in hyperparathyroidism can also involve the jaw bones. In general, the lamina dura vanishes and blurring of the trabecular bone pattern appears as ground glass.[2] Bicortical bony accumulation seems to be less prevalent as an expression of metabolic bone disease. We present a case in which secondary hyperparathyroidism caused bicortical mandibular expansion and intermittent pain in the chin region. Several authors have described cases of bone pain caused by hyperparathyroidism.[3,4] However, the radiographic image mostly indicate bone demineralization, as in the case of maxillofacial brown tumors. In our case bone pain presented with hyperostosis. We would like to raise attention to this atypical oral manifestation of hyperparathyroidism, because it should be included in the broad differential diagnosis in patients with orofacial pain.

CASE REPORT

A 32-year old male patient presented with complaints of recurrent chronic pain in the mandible, especially the chin and submental region. The pain had a sudden onset, without specific aggravating triggers, and it disappeared after several hours to days to recur a few weeks later. This pattern was self-repeating over the preceding 3.5 years. The dull pain did not radiate and wasn't neurogenic in origin, and it responded well to ibuprofen intake (600 mg 3 times a day). The latter was prescribed by his general practitioner. The patient had no other complaints. He did not suffer any allergies or take any other medication. He had smoked for several years. The dental and family histories were insignificant.

On clinical examination no abnormalities were found (Figure 1). There was no intraoral evidence of pathologic conditions, but some enlarged lymph nodes were palpable in the left and right submandibular regions. These were nontender, soft, and mobile. There was no actual clinical evidence of submental adenopathy, but an enlarged submental node had been excised 1 year earlier. The microscopic analysis revealed no pathologic alterations.

To rule out a dental or periodontal cause, panoramic radiography was performed. The cortical density of the mandibular lower border was markedly increased,

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Fig. 1. Normal intraoral appearance.

especially in the region between the mental foramen, as well as in the maxillary canine region (Figure 2). The patient had no complaints in the latter region. Cone beam computed tomography (CT) confirmed the presence of a thickened mandibular cortical layer (Figure 2).

At first sight, there was no obvious intraoral etiology to explain the patient's complaint or the hyperdense aspect of the mandibular lower border. Therefore, skeletal bone scintigraphy was performed. 99mTc-MDP scintigraphy indicated increased tracer uptake in the anterior mandible and maxilla. Single-photon emission CT (SPECT), which combines metabolic and anatomic information, confirmed the osteoblastic hyperactivity in the mandible and ruled out any soft tissue involvement (Figure 3). Although enlarged lymph nodes were palpable and visualized on CT, they did not have hyperactivity on SPECT.

The augmented metabolic activity can have several causes. To rule out any benign (e.g., fibrous dysplasia) or malignant neoplasm, a biopsy of the mandibular lower border was performed in the region of greatest tracer uptake. The specimen confirmed the increased density of cortical bone without evidence of inflammation or cytologic atypia (Figures 4 and 5).

Because the initial clinical and radiologic investigation raised the suspicion of a metabolic disease, a blood analysis was performed. It revealed an increased level of PTH (75.4 ng/L, normal range 14.9-56.9 ng/L) and decreased level of 25-OH-vitamin D (10.2 µg/L, normal range 11.0-60.0 µg/L), as well as decreased serum calcium and normal renal function. Liver tests and the serum phosphate level were normal. Therefore, the patient was diagnosed with secondary hyperparathyroidism caused by hypovitaminosis D. An oral vitamin D supplement (D-Cure, cholecalciferol) was prescribed. As advised by our colleagues of the department of endocrinology, the treatment regimen consisted of 1 peroral ampulla (25,000 U/mL) every 2 weeks during the first month, followed by 1 ampulla per month for the next 3 months. Six weeks later, the patient reported a complete disappearance of all complaints. The pain never recurred in the following 6 months.

DISCUSSION

Hyperparathyroidism was first described by Von Recklinghausen in 1891, presenting its systemic effects. Already in 1945, Weinmann[5] reported the oral manifestations of hyperparathyroidism in the mandible. Hyperparathyroidism predominates in women, with a general male:female ratio of 1:1.7. The average age of patients with hyperparathyroidism is 34.02 years,[6] but patients with secondary hyperparathyroidism may be slightly younger.

PTH controls serum calcium levels by stimulating osteoclastic bone resorption. Excessive hormone release leads to primary, secondary, or tertiary hyperparathyroidism depending on the etiology. Secondary reactive hyperparathyroidism originates from a lack of serum vitamin D and/or calcium, which can be caused by renal failure, intestinal malabsorption, and/or lack of vitamin D/calcium in the diet. It is typically caused by chronic renal failure, mostly related to diabetes mellitus and hypertension.

In secondary hyperparathyroidism, the serum level of PTH is increased, together with hypocalcemia and hyperphosphatemia, which differentiates it from primary and tertiary hyperparathyroidism. Moreover, if alkaline phosphatase is elevated, it indicates high bone turnover. The latter may also be present in Paget disease.[7]

Approximately 8%-16% of the worldwide population suffers from a chronic kidney disease,[8] and 4.3% of them present with craniofacial brown tumors as a manifestation of hyperparathyroidism.[9] The systemic symptoms of hyperparathyroidism are described as "stones, bones, groans, with psychiatric overtones."[6] In our patient, the primary complaint was prolonged jaw pain without evidence of chronic kidney disease. In a recent systematic review, the incidence of oral pain in patients with hyperparathyroidism was 14.0%. However, the most common reported symptom of hyperparathyroidism is facial asymmetry or swelling (78.0%), followed by oral pain and systemic symptoms (11.7%).[6] Bone expansion can be present with and without brown tumors.[10] Other oral manifestations include neuropathy, postextraction complications, periodontitis, and tooth mobility.[6] Periodontitis may not be caused by hyperparathyroidism but possibly be exacerbated by it.[10,11] A brown tumor is common in hyperparathyroidism, especially in the mandible of female patients with the primary form, though it is also found in secondary, and more seldom in tertiary, hyperparathyroidism. Cecchetti et al.[9] reported a serum PTH level >1000 pg/mL (normal range 10-55 pg/mL) in all patients with craniofacial brown tumors.

Occasionally, patients can present with a mandibular fracture, as reported in a patient with primary

Fig. 2. Orthopantomogram and cone beam computed tomography revealed a dense mandibular lower border.

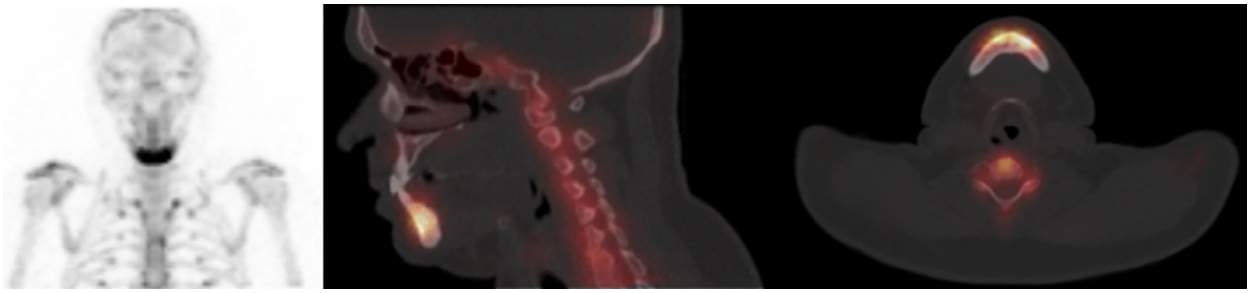

Fig. 3. Skeletal scintigraphy revealed increased tracer uptake in the mandibular chin region. Single-photon emission computed tomography confirmed the bony etiology and ruled out any soft tissue involvement.

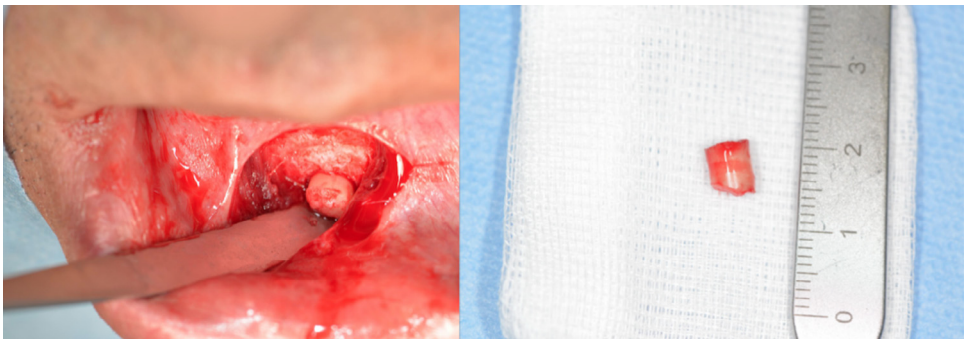

Fig. 4. A bony biopsy of the mandibular lower border was taken at the mental region.

hyperparathyroidism.[12] Giant cell epulis and Sagliker syndrome are also possible manifestations. The mandible is more often affected than the maxilla, but bimaxillary manifestation is common as well.[6] In the present patient, an excessive hypercorticalization of the mandibular lower border was visualized on the panoramic radiograph and cone beam CT. Table I lists reported cases of hyperparathyroidism causing facial pain. In contrast to our patient, bony hypercorticalization wasn't reported in any of these cases.[4,13-21] Because hypercorticalization is not a typical oral manifestation of hyperparathyroidism, extensive technical investigations to rule out other etiologies were performed. The most common reported radiologic feature of hyperparathyroidism is a loss of the lamina dura in 7%-46% of cases.[22-24] However, this should not be considered a pathognomonic sign. Other radiographic features that have been reported are a decreased cortical thickness at the mandibular angle,[25] cortical destruction, tooth displacement, root resorption, obliteration of the mandibular canal, and dystrophic calcifications.[6]

A salt-and-pepper appearance of the skull can be found on skull radiography, but it wasn't performed in this patient. Skeletal scintigraphy and positron emission tomography CT were ordered to rule out other foci of metabolic hyperactivity, but lesions were found only in the anterior mandible and, to a lesser extent, maxilla. However, these imaging modalities cannot distinguish among hyperparathyroidism, skeletal metastasis, osteitis fibrosa, Paget disease, and fibrous dysplasia,[6,26,27] so

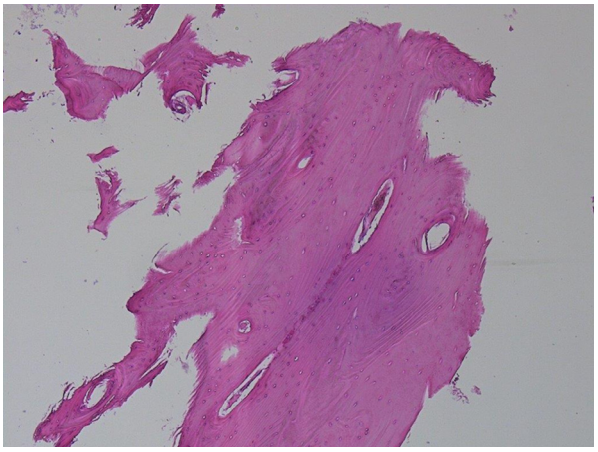

Fig. 5. Biopsy specimen composed of dens cortical bone. The bone is predominantly lamellar, partially woven, without further abnormalities.

their main goal is to locate pathologic lesions to guide further investigations.

There are several treatment modalities, depending on the type of hyperparathyroidism. Parathyroidectomy is the only definitive treatment for primary hyperparathyroidism.[28] For secondary hyperparathyroidism, treatment involves reduction of the dietary phosphorus intake and controlling PTH levels via calcimimetics and vitamin D metabolites. Parathyroidectomy is only performed if the pharmacotherapeutic treatment fails.[29] Tertiary hyperparathyroidism can be treated by parathyroidectomy or with drugs such as cinacalcet, with lower success rates for the latter.[30] In the present patient, the hypocalcemia, hyperparathyroidism, and associated oral pain were successfully treated with oral vitamin D and calcium supplementation. Oral vitamin D substitution is reported as an effective treatment for hypovitaminosis D. Moreover, it can decrease the serum PTH level and restore it within normal ranges.[31,32] This is especially true when serum vitamin D levels are low.[32]

As far as we know, there is no standard vitamin D supplementation regime in patients with hypovitaminosis D–induced hyperparathyroidism and a normal renal function. One should always take in account the serum vitamin D level, renal function, and the patient's gastrointestinal absorption (e.g., after bariatric surgery) when prescribing vitamin D supplementation therapy.

Early detection is important to prevent long-term hypercalcemia and avoid deleterious cardiovascular and skeletal effects,[28] as found in hemodialysis patients with serum calcium levels >10 mg/dL.[29]

CONCLUSION

Though it mostly causes bony demineralization, secondary hyperparathyroidism can also cause mandibular pain and hypercorticalization. Mandibular hypercorticalization, as revealed by radiologic investigation, is not a typical manifestation of hyperparathyroidism.

Table I. Case reports presenting hyperparathyroidism as a cause of pain

Author	*Primary complaint*	*Pain*	*Radiology*	*Diagnosis*	*HyperPTH type and cause*
Masson et al.[13]	Mandibular swelling	Yes	Brown tumor	Brown tumor	Primary—carcinoma
Guney et al.[14]	Palatal swelling Chewing problems	Yes	Eroding mass	Brown tumor	Primary—adenoma
Sutbeyaz et al.[15]	Palatal swelling Mandibular swelling	Yes	Cystic palatal mass	Brown tumor	Primary—adenoma
Jafari-Pozve et al.[4]	Bony pain Swelling of the cheeks	Yes	Multiple radiolucencies	Brown tumor	Secondary—renal failure
Vardhan et al.[16]	Maxillary swelling Pain	Yes	Loss of lamina dura Ground-glass trabecular pattern Maxillary radiolucency	Giant cell lesion	Primary—adenoma
Jakubowski et al.[17]	Mandibular edema Pain Intra-oral nightly bleeding	Yes	Unilocular radiolucency Obliterated mandibular canal Displaced molars	Brown tumor	Secondary—renal failure
Devresse et al.[18]	Painfull swelling of the Mouth floor	Yes	Osteolytic mandibular lesion	Ossifying fibroma	Secondary—renal failure
Magalhães et al.[19]	Mandibular molar Pain	Yes	Ground glass trabecular pattern Osteolytic lesions	Brown tumors	Tertiary—renal transplant
Nair et al.[20]	Mandibular swelling	Yes	Lytic lesion Outer cortex sclerosis	Brown tumor	Secondary—vitamin D deficit
Verma et al.[21]	Pain Facial swelling	Yes	Loss of lamina dura Ground-glass trabecular pattern Multilocular radiolucencies Bicortical expansion	Brown tumor	Secondary—renal failure

hyperPTH, hyperparathyroidism.

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